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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,214	12/01/2003	Muraleedharan G. Nair	MSU 4.1-672	4443

21036 7590 04/27/2006

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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,214	NAIR ET AL.	
	Examiner	Art Unit	
	Michele Flood	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on January 30, 2006. Further acknowledgment is made of Applicant's cancellation of Claims 3 and 4 and newly submitted Claims 6 and 7.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 and 5-7 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1, as amended, Claim 5 and newly added Claims 6 and 7 is/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method for inhibiting the proliferation of colon cancer cells and stomach cancer cells comprising contacting the cells with an effective amount of a composition consisting essentially of malvidin, does not reasonably provide enablement for a method for *in vivo* inhibition in a mammal of proliferation in the stomach, colon and in both the stomach and colon of caner cells which comprises providing an effective amount of malvidin as an active ingredient to the mammal so as to inhibit the proliferation of the cells. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to a method for *in vivo* inhibition in a mammal of proliferation in the stomach, colon and in both the stomach and colon of caner cells which comprises providing an effective amount of malvidin as an active ingredient to the mammal so as to inhibit the proliferation of the cells. The claims are further directed to the method of claim 1 wherein the cells are in a mammal and the malvidin is feed orally to the mammal. The claims are further directed to the composition of claim 1 wherein the composition is in a pharmaceutical carrier; and wherein the stomach cell is AGS and the colon cell is HCT 156 both as maintained by the American Type Culture Collection.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2D 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

While Applicant has reasonably disclosed an *in vitro* method for inhibiting the proliferation of colon (HCT-116) and stomach (AGS) cells comprising incubating the American Type Culture Collection (Rockville, MD) human cancer cell lines in the presence of malvidin, Applicant has not demonstrated an *in vivo* method comprising orally administering an effective amount of the claim-designated composition to a mammal to provide the claimed beneficial functional effect for the inhibition of the proliferation in either the stomach or the colon, much less in both the stomach and the

colon, of cancer cells comprising providing an effective amount of a composition consisting essentially of malvidin, and wherein the malvidin is fed orally to the mammal , as broadly claimed by Applicant. For example, at [0043] of the present application, Applicant discloses, "Malvidin and pelargonidin were in particular found to be excellent inhibitors of stomach and colon cancer cell lines *in vitro*. " However, nowhere in the present specification, as originally filed, does Applicant disclose a method comprising the oral administration of an effective amount of a composition consisting essentially of malvidin to a mammal in need thereof to inhibit the proliferation of either stomach or colon cancer cells therein the mammal or data there from. Instead, Applicant discloses an *in vitro* method for the inhibition of the proliferation of colon (HCT) and stomach (AGS) cells comprising contacting the human cancer cell lines in the presence of dose amounts of malvidin. Given the limited data as to the cancer model used to assess the efficacy of the disclosed composition and the limited disclosure other than the mere mention that the disclosed compositions were inhibitors of stomach and colon cancer cell lines in vitro, it seems highly unlikely that one of skill in the art would be able to use the claim-designated composition as a method for inhibiting the proliferation in a mammal of either stomach or colon cancer cells comprising providing the mammal with an effective amount of a composition consisting essentially of malvidin, even after extensive experimentation.

It should also be noted that the state of the art at the time of filing of the present specification suggested that the delivery of therapeutic drugs which exhibit anti-tumor activity in cancer models do not necessarily have the same beneficial functional effect in humans as disclosed by Fredic Golden (Gorman, Christine. Cancer, "How to tell the hype from the hope: A Special Report", Time, 1998, pages 37-46.) and as disclosed by Trisha Gura ("Cancer Models: Systems for Identifying New Drugs are Often Faulty",

Science, 1997, Vol. 278, pages 1041-1042.). Gura further discloses various different cancer models other than murine cancer models that are not predictive of the anti-cancer activity of potential anticancer agents when delivered to humans. In another instance, Jain (Jain, Rakesh K., "Delivery of molecular medicine to solid tumors", Science (1996), Vol. 271, pages 1079-1080.) discloses that while promising chemotherapeutic agents exhibit activity against cancer cells *in vitro* and *in vivo* tumor systems, these same agents heralded as breakthrough drugs do not have the same functional effect in humans when delivered to humans bearing tumors. Moreover, while Applicant discloses malvidin as an inhibitor of colon cells, Katsube et al. teaches, "Only pure delphindin and the glycoside isolated from the bilberry extract, but not malvidin and the glycoside, inhibited the growth of HCT 116 cells".

There is no guidance in the specification, other than the aforementioned examples directed to an *in vitro* method for inhibiting the proliferation of human cell lines of stomach and colon cancer comprising contacting the cells with a dose amount of a composition consisting essentially of malvidin. Given the insufficient guidance in the specification as to how to carry out the instantly claimed invention, the lack of working examples, the lack of correlative working examples, and the state of the art at the time the specification was filed, the claimed method for the inhibition of the proliferation of either or both of stomach and colon cancer cells in a mammal comprising the administration of an effective amount of the claim-designated composition would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

Accordingly, it would take undue experimentation without a reasonable expectation of success for one skill in the art to provide the claimed method for in vivo inhibition in a mammal of proliferation in the stomach, colon and in both the stomach

and colon of cancer cells comprising providing the mammal with an effective amount of a composition consisting essentially of malvidin to inhibit the proliferation of the cancerous cells, as broadly claimed by Applicant.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 7 recite the limitation "The composition of Claim 1", in line 1. There is insufficient antecedent basis for this limitation in the claims, as the invention of Claim 1 is directed to a method, wherein the composition is administered to a mammal, and wherein the stomach cancer cell or the colon cancer cell is in a mammal.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele Flood
Primary Examiner
Art Unit 1655

MCF
April 15, 2006

MICHELE FLOOD
PRIMARY EXAMINER